REMARKS

STATUS OF THE CLAIMS.

Claims 19, 20, 22, and 27-40 are pending with entry of this amendment. Claims 21, 23, and 26 are canceled without prejudice, and claims 31-40 are added. Claim 19 and its dependent claims have been amended to recite that the claimed antibodies, or antibody fragments, are "purified." Support for this amendment is found in the specification at least at page 33, line 38.

Claims 19 and 29 are amended to recite that the claimed antibody or fragment thereof "binds to a gp120 epitope bound by" monoclonal antibody 5B3," "blocks CD4/gp120 binding and reduces reverse transcriptase activity *in vitro*." This amendment identifies the specific characteristics that the antibody or fragment thereof shares with monoclonal antibody 5B3. Support for this amendment can be found throughout the specification; *see, e.g.,* page 5, lines 17-20, which identifies the characteristics of the monoclonal antibodies of the invention, taken with Table 3, on page 58, and Table 4, on page 61, which indicate the characteristics of monoclonal antibody 5B3. Claims 20, 22, and 26-30 are amended to even more clearly recite the invention.

New claim 31 finds support in former claim 20, as do new claims 33 and 34. New claim 32 finds support in claim 22. New claims 35 and 36 find support in claim 30. New claims 37-40 relate to antibodies or hybridomas related to monoclonal antibodies monoclonal antibodies10D8, 10F6 and 11G5, produced by hybridomas with ATCC accession nos. CLR 10513, CLR 10512, and CLR 10511. Support for these claims are found in the previously pending claims and throughout the specification. *See, e.g.*, page 39, lines 31-35; page 43, lines 4-29; page 62, lines 1-9. Therefore, these amendments introduce no new matter.

INFORMATION DISCLOSURE STATEMENT.

The Examiner indicated that certain references listed on the Information Disclosure Statement filed May 26, 2000 could not be located and were therefore not considered. Office Action, page 2. The Examiner stated that Applicants must submit copies of these references in response to the Office Action if consideration was desired. Copies of these references are enclosed herewith, together with a clean copy of the May 26, 2000 IDS, so that the Examiner can indicate that she has considered these references by initialing their citations on the IDS.

SPECIFICATION.

The Examiner found that the title of the invention was not sufficiently descriptive. Office Action, page 3. Applicants have addressed this objection by amending the title to read: "HIV env Antibodies."

The Examiner objected to the abstract on the ground that it did not reflect the concepts claimed. The abstract has now been amended to describe the subject matter of the pending claims.

The specification was objected to for failing to adhere to the requirements of the sequence rules. This objection is traversed, as it is believed that the sequence rules do not apply to the present application. M.P.E.P. § 2421.01 states: "Compliance [with the sequence rules] is required for most disclosures of sequence data in new applications filed on or after October 1, 1990." As the present application claims the benefit of priority through a chain of continuation/divisional applications extending back to an original application filed on April 3, 1990, Applicants submit that the present application is not a "new" application filed on or after October 1, 1990. Withdrawal of the objection is therefore respectfully requested.

DRAWINGS.

The Examiner objected to Figure 4 for informalities. Office Action, page 3. A complete set of formal drawings accompanies this Amendment.

PRIORITY.

The Examiner noted that the Cross-Reference to Related Applications should be updated to reflect the current status of the related applications. Office Action, page 3. This amendment has been made, and Applicants have requested a Corrected Filing Receipt, as the Examiner suggested.

CLAIM OBJECTIONS.

The Examiner objected to claims 20 and 21 because these claims included the word "and" in all capital letters. Office Action, page 4. This informality has been corrected in claim 20, and claim 21 has been canceled. Withdrawal of this objection is therefore respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 101.

Claims 19 and 26 were rejected under 35 U.S.C. § 101 as drawn to non-statutory subject matter. Office Action, page 4. Specifically, the Examiner indicated that the claims did not distinguish naturally occurring antibodies and suggested amending the claims to recite "isolated" or "purified" antibodies or antibody fragments. The rejection has been overcome by canceling claim 26 and amending claim 19 to recite that the antibodies or fragments thereof are "purified."

REJECTIONS UNDER 35 U.S.C. § 112. SECOND PARAGRAPH.

Claims 19 and 26-30 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Office Action, page 5. Specifically, the Examiner indicated that the description of an antibody, or epitope-binding fragment thereof, as "having the characteristics of" one of several recited antibodies was vague. This rejection is moot as to canceled claim 26 and traversed with respect to claims 19 and 27-30.

Of the rejected claims, only claims 19 and 29 are independent, and the phrase "has the characteristics of" appeared only in these claims. Claims 19 and 29 have each been amended to delete this phrase and instead recite three particular characteristics, specifying that the antibody/fragment "binds to a gp120 epitope bound by monoclonal antibody 5B3, produced by a hybridoma with ATCC accession number 10515, wherein said antibody or fragment thereof blocks CD4/gp120 binding and reduces reverse transcriptase activity *in vitro*." As the characteristics that the claimed antibody/fragment must share with monoclonal antibody 5B3 are explicitly recited in the claims, Applicants submit that claims 19 and 26-30 are clear and definite. Withdrawal of the § 112, second paragraph, rejection is therefore respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112. FIRST PARAGRAPH.

Written Description

Claims 19 and 26-30 were rejected under 35 U.S.C. § 112, first paragraph, as failing to satisfy the written description requirement. Office Action, page 5. Specifically, the Examiner contended that "the skilled artisan would be unable to identify an antibody or epitope-binding fragment thereof with the same 'characteristics' as those instantly claimed." *Id.*, page 6.

Applicants submit that the amendment of claims 19 and 29 (the only independent claims among those rejected on this ground) renders this rejection moot. As noted above, claims 19 and 29 relate to an antibody/fragment and a related hybridoma (respectively), wherein the antibody/fragment "binds to a gp120 epitope bound by monoclonal antibody 5B3, produced by a hybridoma with ATCC accession number 10515, wherein said antibody or fragment thereof blocks CD4/gp120 binding and reduces reverse transcriptase activity *in vitro*." Applicants' specification describes the CD4/gp120 binding assay employed to characterize the antibodies of the invention at page 59, line 35 through page 60, line 6. The reverse transcriptase inhibition assay is described at page 60, lines 12-22 of the specification. Applicants submit that this description, together with the results presented in Table 4, on page 61, clearly establishes that Applicants were in possession of the invention with respect to these characteristics.

However, the Examiner contends that "the exact epitopes the instant antibodies bind to is not disclosed." Office Action, page 6. The Examiner notes that Table 3, one page 58, "appears to list the specific amino acid residue(s) that corresponds to the epitope each Mab binds to." *Id.* However, the Examiner states that "there is no numbering provided for which residue listed corresponds to which amino acid within the randomly expressed portions of gp120 or gp160 the antibodies were raised against." *Id.* This statement is not understood. Table 3 indicates that lambda gt11 mapping (carried out as described on page 57, lines 1-10) indicated that monoclonal antibody 5B3 binds to an epitope in the region of gp120 from amino acid residues 60 to 120. In any case, monoclonal antibody 5B3 was deposited in a public depository, as noted on page 43 of the specification. One skilled in the art would readily appreciate that whether or not an antibody/fragment "binds to a gp120 epitope bound by monoclonal antibody 5B3" can be ascertained by obtaining the antibody and assaying for cross-reactivity, as described in Applicants' specification at page 56, lines 31-37. Accordingly, Applicants submit that the specification

adequately describes the characteristics that the recited antibody/fragment must share with monoclonal antibody 5B3 and how to determine these characteristics. Withdrawal of the §112, written description, rejection is therefore respectfully requested.

Enablement

Claims 19-23 and 26-30 are rejected under §112, first paragraph, as failing to comply with the enablement requirement. This rejection is moot as to canceled claims 21, 23, and 26 and traversed with respect to claims 19, 20, 22 and 27-30. This rejection is based on claims' recitation of monoclonal antibodies and related hybridomas and the documentation of record concerning the deposit of these hybridomas. Office Action, page 8. First, the Examiner noted that, whereas the claims and ATCC deposit receipt list "13H8" as corresponding to one of the deposited hybridomas, the Statement Regarding Deposit of Biological Material Pursuant to 37 C.F.R. §§ 1.804(a) and 1.808(a)(2) refers to "13HB." As the Examiner concluded, this designation in the Statement represents a typographical error. This Amendment is therefore accompanied by a replacement Statement in which this error is corrected.

Second, as the Examiner pointed out, claims 19 and 29 recited that monoclonal antibody 6D8 was produced by a hybridoma with ATCC accession number CRL 10513, whereas the Statement indicated that CRL 10513 corresponds to monoclonal antibody "10D8." *Id.* This issue is moot, as none of the currently pending claims recite monoclonal antibody 6D8.

Third, the Examiner noted that the record contains no indication that hybridomas corresponding to monoclonal antibody 5B6, which was previously recited in the claims. *Id.*, page 9. To overcome this rejection, the claims have been amended to recite antibodies and hybridomas corresponding to three of the deposited hybridomas, namely those producing monoclonal antibodies 5B3, 6E10, and 13H8.

Claims 21-23 were additionally rejected for alleged lack of enablement on the ground that the specification "does not reasonably provide enablement for inducing a therapeutic or prophylactic immune response against HIV with these antibodies. *Id.*, page 11. This rejection is moot as to claims 21 and 23, which have been canceled. Claim 22 recites: "The monoclonal antibody of claim 20, wherein said monoclonal antibody is conjugated to a toxin." The specification describes such "immunotoxins" at page 34, line 22 through page 37, line 9. At page 36, lines 24-29, the specification describes the use of immunotoxins "to kill infected human cells *in vitro* for

diagnostic purposes." Applicants submit that this description in the specification enables the use of the monoclonal antibody of claim 22, which is conjugated to a toxin, in an *in vitro* diagnostic assay.

As the specification fully enables those skilled in the art to practice the subject matter of the pending claims, withdrawal of the § 112, enablement, rejection is respectfully requested.

REJECTIONS UNDER 35 U.S.C. §102.

Berman

Claims 19 and 26 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Berman *et al.* (Journal of Virology (1989) 63:3489-98). Office Action, page 15. This rejection is moot as to claim 26, in light of its cancellation, and traversed with respect to claim 19.

Claim 19 recites a "purified monoclonal antibody, or epitope-binding fragment thereof." Berman teaches polyclonal antisera prepared against various HIV envelope proteins, not a purified monoclonal antibody or fragment thereof. Berman, page 3491, col. 1. In addition, claim 19 recites that the purified monoclonal antibody or fragment thereof "binds to a gp120 epitope bound by monoclonal antibody 5B3, with ATCC accession number 10515." Berman is devoid of any basis for concluding that any of the antibodies in the disclosed polyclonal antisera bind to this epitope. Claim 19 further recites that the claimed "antibody or fragment thereof blocks CD4/gp120 binding and reduces reverse transcriptase activity *in vitro*." As the Examiner pointed out, Berman's antisera exhibited these characteristics; however, Berman fails to teach that these characteristics are found in a single antibody or fragment thereof. For at least these reasons, Berman fails to anticipate claim 19.

Lasky

Claims 19 and 26 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lasky *et al.* (Cell (1987) 50:975-985). Office Action, page 16. This rejection is moot as to cancelled claim 26 and traversed with respect to claim 19.

The rejection was based on the Examiner's contention that "Lasky et al. teach monoclonal antibodies, 5C2E5 and 7F11, that block the interaction between gp120 and the CD4 receptor." *Id.* As noted above, claim 19 recites a monoclonal antibody or fragment thereof that "binds to a gp120 epitope bound by monoclonal antibody 5B3, with ATCC accession number 10515." Table 3, on page 58 of Applicants' specification indicates that this antibody binds to HTLV

IIIB residues 60-120 and not to a fragment spanning residues 390-439 (which the table shows was bound by monoclonal antibody 5C2). By contrast, Lasky teaches that the disclosed antibodies bound to an epitope within residues 397-349 of HTLV IIIB. *See* Lasky, page 978, col. 2, taken with page 983, col. 1 (establishing that these researchers were working with the IIIB strain). Furthermore, Lasky fails to disclose whether monoclonal antibodies 5C2E5 and 7F11 reduce reverse transcriptase activity *in vitro*, as required for the antibody/fragment of claim 19. Therefore, Lasky fails to anticipate claim 19.

Matsushita

Claims 19 and 26 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Matsushita *et al.* (Journal of Virology (1988) 62:2107-14). Office Action, page 16. This rejection is moot as to cancelled claim 26 and traversed with respect to claim 19.

Matsushita discloses the preparation of a gp120 specific monoclonal antibody termed "0.5β." Matsushita, page 2108, col. 2. Matsushita teaches that this antibody bound to a 24-amino acid-long peptide from the HTLV IIIB strain (among others) that included residues 308-331. *See* Matsushita, page 2112, Fig. 6. The rejection is apparently based on the contention that this antibody binds to the same epitope as the antibody/fragment of claim 19. *See* Office Action, page 16 (citing Matsushita, Fig. 6.) However, the antibody/fragment of claim 19 "binds to a gp120 epitope bound by monoclonal antibody 5B3." Monoclonal antibody 5B3 binds to HTLV IIIB residues 60-120 and not to a fragment spanning residues 301-324 (which the table shows was bound by monoclonal antibodies 10D8, 10F6, and 11G5). Thus, Matsushita fails to teach or suggest a monoclonal antibody that "binds to a gp120 epitope bound by monoclonal antibody 5B3," as recited in claim 19. Furthermore, claim 19 recites that the claimed "antibody or fragment thereof blocks CD4/gp120 binding and reduces reverse transcriptase activity *in vitro*." Matsushita *et al.* neither teach nor suggest that the disclosed antibody had either of these characteristics. Accordingly Matsushita fails to teach a monoclonal antibody having any of the characteristics recited in claim 19.

Javaherian

Claims 19 and 26 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Javaherian *et al.* (PNAS (1989) 86:6768-72). Office Action, page 17. This rejection is moot as to cancelled claim 26 and traversed with respect to claim 19.

Claim 19 recites a "purified monoclonal antibody, or epitope-binding fragment thereof." Javaherian teaches polyclonal antisera prepared against various HIV envelope proteins, not a purified monoclonal antibody or fragment thereof. Javaherian, page 6769 col. 2 – page 6770, col. 2. In addition, the antibody/fragment of claim 19 "binds to a gp120 epitope bound by monoclonal antibody 5B3," which binds to HTLV IIIB residues 60-120. Javaherian contains no evidence that any of the antibodies in the disclosed polyclonal antisera bind to this epitope. Indeed, as the Examiner noted, this report focuses on a "principal neutralizing determinant" (the "RP135 determinant") located in the region spanning HTLV IIIB residues 307-335. Claim 19 further recites that the claimed "antibody or fragment thereof blocks CD4/gp120 binding and reduces reverse transcriptase activity *in vitro*." Javaherian *et al.* demonstrated that the disclosed antisera reduced reverse transcriptase activity *in vitro*, but the authors did not test whether these antisera blocked CD4/gp120 binding. However, Javaherian states: "Antibodies bound to the RP135 determinant do not block binding of gp120 to CD4." Javaherian, page 6772. Thus, if anything Javaherian indicates that the disclosed antisera do no have this characteristic. Moreover, there is simply no evidence that that the characteristics recited in claim 19 are found in a single antibody or fragment thereof in the Javaherian antisera. For at least these reasons, Javaherian fails to anticipate claim 19.

Dowbenko

Claims 19-22 and 26-28 were rejected under 35 U.S.C. 102(b) as allegedly anticipated by Dowbenko *et al.* (Journal of Virology (1988) 62:4703-11). Office Action, page 17. This rejection is moot as to canceled claims 21 and 26 and traversed with respect to claim 19, 20, 22, 27, and 28.

Of the rejected claims, only claims 19 and 20 are independent. In explaining the rejection, the Examiner relies on Dowbenko's teaching of an anti-gp120 antibody termed "6D8." *Id.* Applicant note that, as amended, neither claim 19, nor 20 refers to monoclonal antibody 6D8.

As discussed above, claim 19 relates to a purified monoclonal antibody or fragment thereof that has particular characteristics of monoclonal antibody 5B3, including binding to a gp120

epitope bound by 5BE, blocking of CD4/gp120 binding, and reduction of reverse transcriptase activity *in vitro*. Dowbenko discloses three monoclonal antibodies specific for gp120 that "were found to block the interaction between gp120 and CD4." Dowbenko, page 4705, col. 2. These were termed: 5C2, 7F11, and 7G11. *Id.* Epitope mapping studies indicated that these three antibodies bound to an epitope within HTLV IIIB residues 296-471 and not to an epitope within residues 1-295. The antibody/fragment of claim 19 must share an epitope with Applicants' monoclonal antibody 5B3, which binds to HTLV IIIB residues 60-120. Thus, the antibody/fragment of claim 19 is clearly distinguished from all of Dowbenko's CD4-blocking antibodies, based on epitope binding. In addition, nothing in Dowbenko teaches that any of the CD4-blocking antibodies has the ability to reduce reverse transcriptase activity *in vitro*, as recited in claim 19. Claim 19 is therefore distinguished from Dowbenko for this additional reason.

Claim 20 recites: "A monoclonal antibody, selected from the group consisting of monoclonal antibodies 5B3, 6E10, and 13H8, produced by hybridomas with ATCC accession nos. 10515, 10514, and 10510, respectively." Dowbenko is devoid of any reference to these specific monoclonal antibodies. In addition, each of the claimed antibodies blocks CD4/gp120 binding and inhibits reverse transcriptase activity *in vitro*. Applicants' specification, page 61, Table 4. As noted above, Dowbenko fails to teach that any disclosed CD4-blocking antibody can also inhibit reverse transcriptase. Accordingly, Dowbenko fails to anticipate independent claims 19 and 20, and claims 22, 27, and 28 are distinguished from Dowbenko at least by virtue of their dependence from one of these two claims.

Remington

Claims 19-21 and 26 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Remington *et al.* (U.S. Patent No. 4,361,647). Office Action, page 18. This rejection is moot as to canceled claims 21 and 26 and traversed with respect to claims 19 and 20.

Remington was cited for its disclosure of a monoclonal antibody termed "5B6." *Id.* As amended, neither claim 19, nor claim 20 refers to monoclonal antibody 5B6. In explaining the rejection, the Examiner stated: "Since the characteristics intended in claim 19 are indeterminable, the monoclonal antibody of Remington appears to possess the characteristics required by the claim." *Id.*, page 18. As amended, claim 19 recites particular characteristics of monoclonal antibody 5B3, including binding to a gp120 epitope bound by 5BE, blocking of CD4/gp120 binding, and reduction

of reverse transcriptase activity *in vitro*. Remington's antibodies are specific for *Toxoplasma gondii* antigens, not gp120. Remington, col. 8, lines 49-50. It is thus extremely unlikely that Remington's antibodies possessed any of the characteristics recited in claim 19, much less all three.

Claim 20 recites: "A monoclonal antibody, selected from the group consisting of monoclonal antibodies 5B3, 6E10, and 13H8, produced by hybridomas with ATCC accession nos. 10515, 10514, and 10510, respectively." Remington is devoid of any reference to these specific monoclonal antibodies. In addition, each of the claimed antibodies is an anti-gp120 antibody that blocks CD4/gp120 binding and inhibits reverse transcriptase activity *in vitro*. Applicants' specification, page 61, Table 4. Because Remington's antibodies are not directed against gp120, it is unlikely that Remington's antibodies share any of the antigen-specific characteristics of the claimed antibodies.

As the pending claims clearly distinguish all of the cited references, withdrawal of the § 102 rejections is respectfully requested.

REJECTIONS UNDER 35 U.S.C. §103.

Dowbenko

Claim 30 was rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Dowbenko *et al.* Office Action, page 18. This rejection is respectfully traversed.

Claim 30 recites: "A hybridoma selected from the group consisting of hybridomas with ATCC accession numbers 10515, CRL 10514, CRL and 10510." These hybridomas correspond to monoclonal anti-gp120 antibodies 5B3, 6E10, and 13H8, respectively.

The rejection is based on Dowbenko's disclosure of a monoclonal antibody termed "6D8." None of the hybridomas recited in claim 30 produces a "6D8" antibody. Furthermore, all of the hybridomas produce antibodies that block CD4/gp120 binding and inhibit reverse transcriptase activity *in vitro*. Applicants' specification, page 61, Table 4. As Dowbenko fails to teach or suggest that any disclosed CD4-blocking antibody can also inhibit reverse transcriptase, Dowbenko fails to teach or suggest hybridomas, such as those recited in claim 30. Withdrawal of the § 103 rejection over Dowbenko is therefore respectfully requested.

Remington and Reading

Claim 22 was rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Remington, in view of Reading (U.S. Patent No. 4,474,893). Office Action, page 18. The rejection is respectfully traversed.

Claim 22 depends from claim 20, which recites: "A monoclonal antibody, selected from the group consisting of monoclonal antibodies 5B3, 6E10, and 13H8, produced by hybridomas with ATCC accession nos. 10515, 10514, and 10510, respectively." Claim 20 is distinguished from the primary reference, Remington, on the ground that Remington fails to teach or suggest the claimed anti-gp120 antibodies.

Claim 22 recites that the monoclonal antibody of claim 22 is conjugated to a toxin. The Examiner acknowledges that Remington does not teach conjugating a monoclonal antibody to a toxin and cites Reading for this teaching. Office Action, page 18. However, Reading does not remedy the failure of Remington to teach or suggest the claimed anti-gp120 antibodies. In particular, Remington teaches specific monoclonal antibodies directed to *T. gondii* antigens, and Reading teaches no specific monoclonal antibodies. Accordingly, the Remington-Reading combination fails to teach or suggest the monoclonal antibody of claim 22. Withdrawal of the § 103 rejection over these references is therefore respectfully requested.

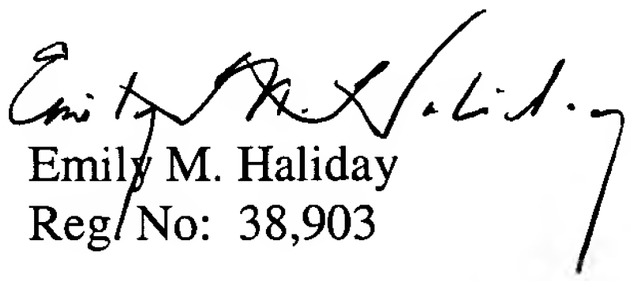
CONCLUSION.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Amendment, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 769-3509 to schedule an interview.

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P.O. BOX 458
Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877

Respectfully submitted,



Emily M. Haliday
Reg. No: 38,903